

William F. Dall'Acqua, Ph.D.

Curriculum Vitae

PROFESSIONAL ADDRESS

MedImmune, Inc.
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PERSONAL INFORMATIONS

Date and place of birth:

April 9, 1969, Paris, France

Citizenship:

French

Immigration status in USA:

Permanent Resident

Languages:

English, French and German

EDUCATION

1996: Ph.D. in Immunology with Highest Honors. University of Paris in conjunction with the University of Maryland.

1992: Pre-doctoral Thesis in Biochemistry with Highest Honors. University of Paris in conjunction with the Pasteur Institute.

1991: M.S. in Biochemistry with High Honors. University of Paris.

1990: B.S. in Biochemistry with High Honors. University of Paris.

HONORS AND AWARDS

1993-1996: Doctoral Fellowship from the French Department of Research.

1992: Pre-doctoral Achievement Award. Graduated first in my class.

1991: Pasteur Institute's pre-doctoral Fellowship.

PROFESSIONAL AFFILIATIONS

- Editor of *Methods* (Elsevier publication).

- Primary reviewer of a Site Review Team for the National Cancer Institute (NCI)/National Institutes of Health (NIH).
- Regular reviewer for the Journal of Immunology.
- Member of The American Society for Biochemistry and Molecular Biology (ASBMB), The American Society for Cell Biology (ASCB), The Society for Leukocyte Biology (SLB) and The American Association for the Advancement of Science (AAAS).

RESEARCH EXPERIENCE

04/05-present: Associate Director at MedImmune, Inc., Department of Protein Engineering, Gaithersburg, MD 20878.

- Conception and execution of new protein engineering approaches.
- Conception and execution of new humanization techniques.
- Study of the interaction between primate CD2 molecules and various antibodies.
- Study of the interaction between immunoglobulins and the neonatal Fc receptor (FcRn).

01/02-04/05: Scientist III at MedImmune, Inc., Department of Protein Engineering, Gaithersburg, MD 20878.

10/99-01/02: Scientist II at MedImmune, Inc., Department of Immunology and Molecular Genetics, Gaithersburg, MD 20878.

02/97-10/99: Post-Doctoral Fellow in the laboratory of Dr. Paul Carter, Molecular Oncology Department, Genentech, Inc., South San Francisco, CA 94080.

- Study of the contribution of domain interface residues to the stability of antibody C_H3 domain homodimers.
- Study of human neutrophil elastase. Engineering of its specificity by substrate-assisted catalysis.

09/93-09/96: Ph.D. Thesis research in the laboratory of Professor Roberto J. Poljak, Center for Advanced Research in Biotechnology (CARB), Rockville, MD 20850.

- Study of the molecular basis of two antigen-antibody interactions.

09/91-09/92: Pre-doctoral research training in the laboratory of Professor Roberto J. Poljak, Immunology Department, Pasteur Institute, Paris, France.

- Study of the interaction of lysozyme with anti-lysozyme antibodies and mutants thereof.

PROFESSIONAL SKILLS

Biochemistry/Biophysics:

- Protein purification and characterization using a wide variety of techniques such as chromatography (HPLC, FPLC, IMAC, affinity), analytical electrophoresis, IEF, spectrofluorometry and densitometry.
- Protein crystallization.
- Studies of protein-protein interactions using various assays such as calorimetry, BIAcore, sedimentation equilibrium, fluorescence quenching and equilibrium denaturation.
- Kinetic studies of enzymes.
- Analysis and modeling of protein three-dimensional structures (using Insight II, Midas, Swiss pdb Viewer and POV Ray programs).

Molecular Biology/Immunology:

- Gene cloning, site-directed mutagenesis, PCR, DNA sequencing (manual and automated), vector construction, mRNA isolation.
- Cloning of hybridoma's antibody V_H and V_L genes, generation of monoclonal antibodies.
- Expression of recombinant proteins in *E. Coli*, yeast and mammalian cells.
- Construction, selection and screening of phage/phagemid libraries displaying peptides or antibodies.
- High throughput assays.
- ELISA, FACS, immunoprecipitations, immunodot assays, Western blot.

Cell Culture:

- Bacteriological techniques (including fermentation).
- Culture and manipulation of eukaryotic cells, transfection.
- Cytotoxicity assays (ADCC, CDC).

SCIENTIFIC INTERESTS

- Protein engineering.
- Structure-function analysis of biological molecules.
- Structure-based design of novel therapeutic agents.

PUBLICATIONS

Wu, H. and **Dall'Acqua, W¹**. (2005). Editorial: Humanized Antibodies and Their Applications. *Methods* **36**, 1-2. ¹**Corresponding author**

Dall'Acqua, W¹., Damschroder, M. Zhang, J., Widjaja, L., Yu, G. and Wu, H. (2005). Humanization of antibodies by framework shuffling. *Methods* **36**, 43-60.

¹**Corresponding author.**

Damschroder, M.M, Kozhich, A., Woods, R.M., Cheng, L., Mullikin, B.A., Wilson, S.D., Ulbrandt, N.D., Bachy, C.M., Wu, H., Suzich, J.A., Kiener, P.A., **Dall'Acqua, W¹**. and White, W.I. (2004). Analysis of Human and Primate CD2 Molecules by Protein Sequence and Epitope Mapping with Anti-human CD2 Antibodies. *Molecular Immunology* **41**, 985-1000. ¹**Corresponding author.**

Dall'Acqua, W¹., Woods, R., Ward, S., Palaszynski, S., Patel, N.K., Brewah, Y., Wu, H., Kiener, P.A. and Langermann, S. (2002). Increasing the Affinity of a Human IgG1 for the Neonatal Fc Receptor: Biological Consequences. *The Journal of Immunology* **169**, 5171-5180. ¹**Corresponding author**

Dall'Acqua, W. and Carter, P. (2000). Substrate-Assisted Catalysis: molecular Basis and Biological Significance. *Protein Science* **9**, 1-9.

Dall'Acqua, W., Halin, C., Rodrigues, M.L. and Carter, P. (1999). Human neutrophil Elastase Substrate Specificity Tailored Through 'Substrate-Assisted Catalysis' and Substrate Phage. *Protein Engineering* **12**, 981-987.

Dall'Acqua, W. and Carter, P. (1998). Antibody Engineering. *Current Opinion in Structural Biology* **8**, 443-450.

Dall'Acqua, W., Simon, A., Mulkerrin, M.G. and Carter, P. (1998). Contribution of Domain Interface Residues to the Stability of Antibody C_H3 Domain Homodimers. *Biochemistry* **37**, 9266-9273.

Dall'Acqua, W., Goldman, E.R., Lin, W., Teng, C., Daisuke, T., Li, H., Ysern, X., Braden, B.C, Li, Y., Smith-Gill, S.J. and Mariuzza, R.A. (1998). A mutational Analysis of Binding Interactions in an Antigen-Antibody Protein-Protein Complex. *Biochemistry* **37**, 7981-7991.

Goldbaum, F.A., Velikovsky, C.A., **Dall'Acqua, W.**, Fossati, C.A., Fields, B.A., Braden, B.C, Poljak, R.J. and Mariuzza, R.A. (1997). Characterization of anti-anti-Idiotypic Antibodies that Bind Antigen and an anti-Idiotype. *Proc. Natl. Acad. Sci. USA* **94**, 8697-8701.

Goldman, E.R., **Dall'Acqua, W.**, Braden, B.C. and Mariuzza, R.A. (1997). Analysis of Binding Interactions in an Idiotope-anti-Idiotope Protein-Protein Complex by Double Mutant Cycles. *Biochemistry* **36**, 49-56.

Fields, B.A., Goldbaum, F.A., **Dall'Acqua, W.**, Malchiodi, E.L., Cauerhff, A., Schwarz, F.P., Ysern, X., Poljak, R.J. and Mariuzza, R.A. (1996). Hydrogen Bonding and Solvent Structure in an Antigen-Antibody Interface. Crystal Structures and Thermodynamic Characterization of Three Fv Mutants Complexed with Lysozyme. *Biochemistry* **35**, 15494-15503.

Braden, B.C., Fields, B.A., Ysern, X., **Dall'Acqua, W.**, Goldbaum, F.A., Poljak, R.J. and Mariuzza, R.A. (1996). Crystal Structure of an Fv-Fv Idiotope-anti-Idiotope Complex at 1.9A Resolution. *J. Mol. Biol.* **264**, 137-151.

Dall'Acqua, W., Goldman, E.R., Eisenstein, E. and Mariuzza, R.A. (1996). A Mutational Analysis of the Binding of Two Different Proteins to the Same Antibody. *Biochemistry* **35**, 9667-9676.

Braden, B.C., Fields, B.A., Ysern, X., Goldbaum, F.A., **Dall'Acqua, W.**, Schwarz, F.P., Poljak, R.J. and Mariuzza, R.A. (1996). Crystal Structure of the Complex of the Variable Domain of Antibody D1.3 and Turkey Egg-White Lysozyme: a Novel Conformational Change in Antibody CDR-L3 Selects for Antigen. *J. Mol. Biol.* **257**, 889-894.

Braden, B.C., **Dall'Acqua, W.**, Eisenstein, E., Fields, B.A., Goldbaum, F.A., Malchiodi, E.L., Mariuzza, R.A., Poljak, R.J., Schwarz, F.P., Ysern, X. and Poljak, R.J. (1995). Protein Motion and Key Complementarity in Antigen-Antibody Reactions. *Pharmaceutica Acta Helveticae* **69**, 225-230.

Braden, B.C., Cauerhff, A., **Dall'Acqua, W.**, Fields, B.A., Goldbaum, F.A., Malchiodi, E.L., Mariuzza, R.A., Poljak, R.J., Schwarz, F.P., Ysern, X. and Bhat, T.N. (1995). Structure and Thermodynamics of Antigen Recognition by Antibodies. *Annals of the New York Academy of Sciences* **764**, 315-327.

Ysern, X., Fields, B.A., Bhat, T.N., Goldbaum, F.A., **Dall'Acqua, W.**, Schwarz, F.P., Poljak, R.J. and Mariuzza, R.A. (1994). Solvent Rearrangement in an Antigen-Antibody Interface Introduced by Site-Directed Mutagenesis of the Antibody Combining Site. *J. Mol. Biol.* **238**, 496-500.

Bhat, T.N., Bentley, G.A., Boulot, G., Greene, M.I., Tello, D., **Dall'Acqua, W.**, Souchon, H., Schwarz, F.P., Mariuzza, R.A. and Poljak, R.J. (1994). Bound Water Molecules and Conformational Stabilization Help Mediate an Antigen-Antibody Association. *Proc. Natl. Acad. Sci. USA* **91**, 1089-1093.

PUBLISHED PATENTS

Dall'Acqua, W., Wu, H. and Damschroder, M. (2005). Periplasmic expression of antibodies using a single signal sequence. Application number US20050181479A1.

Wu, H., **Dall'Acqua, W.** and Damschroder, M. (2005). Humanization of antibodies. Application number US20050048617A1.

Wu, H., **Dall'Acqua, W.** and Damschroder, M. (2005). Humanization of antibodies. Application number US20050042664A1.

Reed, J., **Dall'acqua, W.**, Van Snick, J., Renauld, J.C., Cormont, F. and Uyttenhove, C. (2003). Recombinant anti-interleukin-9 antibodies. Application numbers US20030219439A1 and WO03086458A1.

Dall'Acqua, W., Johnson, S. and Ward, S. (2002). Molecules with Extended Half-Lives, Compositions and uses thereof. Application numbers US20030190311A1 and WO02060919A2.

Carter, P., **Dall'Acqua, W.** and Rodrigues, M. (2000). Elastase Variants and Substrates. Application number WO0068363A2.

NEW GENES CLONING

White, W.I., Mullikin,B.A., Wilson, S.D., Kozhich, A.A., Suzich, J.A., Wu, H., Kiener, P.A., Dormitzer, M.M. and **Dall'Acqua, W.F.** Pan troglodytes (chimpanzee), Macaca fascicularis (cynomolgus monkey), Macaca mulatta (rhesus monkey), Macaca nemestrina (pig-tailed macaque), Macaca arctoides (stumped-tailed macaque), Papio anubis (olive baboon), Cercopithecus torquatus atys (african green monkey) and Macaca assamensis (assameese macaque) cluster of differentiation 2 (CD2) mRNA. GenBank accession numbers AY445034, AY445036, AY445037, AY445041, AY445040, AY445035, AY445038 and AY445039, respectively.